Claims

1. A method of obtaining a substantially pure cannabinoid or cannabinoid acid or a product enriched in a given cannabinoid or cannabinoid acid from a plant material, comprising:
i) obtaining an extract containing a cannabinoid or cannabinoid acid from a plant material;
ii) subjecting the extract of step (i) to a chromatographic step to produce a partially purified extract;
iii) dissolving the partially purified extract in a first solvent, removing any insoluble material therefrom and removing the solvent; and
iv) dissolving the product obtained in step iii) in a second solvent, removing any insoluble material therefrom, and removing the solvent to obtain the substantially pure cannabinoid or cannabinoid acid or the product enriched in a given cannabinoid or cannabinoid acid, wherein the first and second solvents are different, and wherein one of the first or second solvents is a solvent which is substantially more polar than the cannabinoid/cannabinoid acid which it is desired to purify, and the other solvent is a solvent which is substantially less polar than the cannabinoid/cannabinoid acid which it is desired to purify.

2. A method according to claim 1 wherein one of the solvents is an alcohol.

3. A method according to claim 2 wherein one of the solvents is methanol.

4. A method according to any one of claims 1 to 3 wherein one of the solvents is a straight or branched chain C5-C12 alkane.

5. A method according to claim 4 wherein one of the solvents is pentane.

6. A method according to claim 5 wherein one of the solvents is pentane and the other solvent is methanol.

7. A method according to any one of the preceding claims wherein the extract containing a cannabinoid or cannabinoid acid obtained in step (i) is prepared by a process comprising solvent extraction of the plant material.

8. A method according to claim 7 wherein step (i) comprises dissolving the plant material in an extraction solvent, removing any insoluble material from the resultant solution and removing the solvent to form an extract containing a cannabinoid or cannabinoid acid.

9. A method according to claim 7 or claim 8 wherein the extraction solvent is a non-polar solvent, ethanol, methanol or carbon dioxide.

10. A method according to claim 9 wherein the non-polar solvent comprises a straight or branched chain C5-C12 alkane.

11. A method according to claim 10 wherein the non-polar solvent is hexane.

12. A method according to claim 7 or claim 8, wherein the extraction solvent is acidified.

13. A method according to claim 12 wherein the extraction solvent is an acidified non-polar solvent.

14. A method according to claim 13 wherein the extraction solvent is an acidified straight or branched chain C5-C12 alkane.

15. A method according to claim 14 wherein the extraction solvent is 0.1% v/v acetic acid in hexane.

16. A method according to any one of claims 1 to 15, which includes a further step, prior to step (i), of decarboxylating the plant material.

17. A method according to any one of claims 1 to 6 wherein the extract containing a cannabinoid or cannabinoid acid obtained in step (i) comprises a botanical drug substance derived from the plant material.

18. A method according to claim 17 wherein the botanical drug substance is prepared by a process comprising solvent extraction of the plant material.

19. A method according to claim 18 wherein the botanical drug substance is prepared by extraction with carbon dioxide.

20. A method according to claim 19 wherein the botanical drug substance is prepared by a process comprising extraction with carbon dioxide (CO_2), followed by a secondary extraction step to remove a proportion of the non-target materials.

21. A method according to claim 20 wherein the secondary extraction step is ethanolic precipitation.

22. A method according to claim 20 or claim 21 wherein the process for preparing the botanical drug substance further includes a charcoal clean-up step.

23. A method according to claim 22 wherein the botanical drug substance is prepared by a process comprising:
i) optional decarboxylation of the plant material,
ii) extraction with liquid CO_2, to produce a crude botanical drug substance,
iii) precipitation with C1-C5 alcohol to reduce the proportion of non-target materials,
iv) removal of the precipitate,
v) treatment with activated charcoal, and

vi) evaporation to remove C1-C5 alcohol and water, thereby producing a final botanical drug substance.

24. A method according to any one of the preceding claims wherein the chromatographic step comprises column chromatography.

25. A method according to any one of the preceding claims wherein the chromatographic step is based on molecular sizing and polarity.

26. A method according to claim 25 wherein the chromatographic step is carried out using a Sephadex™ LH-20 matrix.

27. A method according to claim 26 wherein the chromatographic step is carried out using a 2:1 mixture of chloroform/dichloromethane as solvent.

28. A substantially pure preparation of Δ^9 tetrahydrocannabinolic acid (Δ^9 THCA) having a chromatographic purity of greater than 95%, more preferably greater than 96%, more preferably greater than 97% or most preferably greater than 98% by area normalisation of an HPLC profile.

29. A preparation according to claim 28 which is a pale yellow crystalline solid at room temperature.

30. A preparation according to claim 28 or claim 29 which comprises less than 2%, preferably less than 1.5%, most preferably 1% or less Δ^9 THC (w/w).

31. A preparation according to any one of claims 28 to 30 which comprises less than 2%, more preferably less than 1.5%, more preferably less than 1% or most preferably less than 0.5% CBD (w/w).

32. A preparation according to any one of claims 28 to 31 which comprises less than 2%, more preferably less than 1.5%, or most preferably less than 1% CBN

(w/w).

33. A preparation according to any one of claims 28 to 32 which is obtainable from cannabis plant material using a method comprising:

i) preparing an extract of the cannabis plant material with 0.1% v/v acetic acid in hexane,
ii) filtering the resultant extract and removing solvent from filtrate by rotary evaporation to form an extract enriched in Δ^9 THCA,
iii) passing a solution of the resulting Δ^9 THCA enriched extract through a column packed with Sephadex-LH20™, eluting with 2:1 chloroform/dichloromethane,
iv) collecting Δ^9 THCA rich fractions eluted from the column and removing solvent by rotary evaporation,
v) re-dissolving the crude Δ^9 THCA obtained in step iv) in methanol, removing insoluble residue by filtration and removing solvent from filtrate by rotary evaporation,
vi) re-dissolving the product of step v) in pentane, removing insoluble residue by filtration and removing solvent from filtrate by rotary evaporation to produce Δ^9 THCA crystals.

34. A substantially pure preparation of Δ^9 tetrahydrocannabinolic acid (Δ^9 THCA) substantially as described herein and having an HPLC profile substantially as shown in Figure 2.

35. A substantially pure preparation of cannabidiolic acid (CBDA) having a chromatographic purity of greater than 90%, more preferably greater than 92% or most preferably greater than 94% by area normalisation of an HPLC profile.

36. A preparation according to claim 35 which is a pale yellow crystalline solid at room temperature.

37. A preparation according to claim 35 or claim

36 comprising 5% or less, preferably 4.5% or less, more preferably 4% or less, more preferably 3.5% or less or most preferably 3% or less CBD (w/w).

38. A preparation according to any one of claims 35 to 37 comprising less than 1%, preferably less than 0.8%, more preferably less than 0.6%, more preferably less than 0.4%, more preferably less than 0.2% or most preferably less than 0.1% Δ^9 THCA (w/w).

39. A preparation according to any one of claims 35 to 38 comprising less than 1%, preferably less than 0.8%, more preferably less than 0.6%, more preferably less than 0.4%, more preferably less than 0.2% or most preferably less than 0.1% Δ^9 THC (w/w).

40. A substantially pure preparation of cannabidiolic acid (CBDA) having a chromatographic purity of greater than 94%, more preferably greater than 96% or most preferably greater than 98% by area normalisation of an HPLC profile.

41. A preparation according to claim 40 which is a clear colourless solution at room temperature.

42. A preparation according to claim 40 or claim 41 comprising 3% or less, preferably 2% or less, more preferably 1%, or most preferably less than 0.1% CBD (w/w).

43. A preparation according to any one of claims 40 to 42 comprising less than 0.8%, preferably less than 0.6%, more preferably less than 0.3% Δ^9 THCA (w/w).

44. A preparation according to any one of claims 40 to 43 comprising less than 1%, preferably less than 0.8%, more preferably less than 0.6%, more preferably less than 0.4%, more preferably less than 0.2% or most preferably less than 0.1% Δ^9 THC (w/w).

45. A preparation according to any one of claims 35 to 44 which is obtainable from cannabis plant material using a method comprising:
i) preparing an extract of the cannabis plant material with 0.1% v/v acetic acid in hexane,
ii) filtering the resultant extract and removing solvent from filtrate by rotary evaporation to form an extract enriched in CBDA,
iii) passing a solution of the resulting CBDA enriched extract through a column packed with Sephadex-LH20™, eluting with 2:1 chloroform/dichloromethane,
iv) collecting CBDA rich fractions eluted from the column and removing solvent by rotary evaporation,
v) re-dissolving the crude CBDA obtained in step iv) in methanol, removing insoluble residue by filtration and removing solvent from filtrate by rotary evaporation,
vi) re-dissolving the product of step v) in pentane, removing insoluble residue by filtration and removing solvent from filtrate by rotary evaporation to produce CBDA crystals.

46. A substantially pure preparation of cannabidiolic acid (CBDA) substantially as described herein and having an HPLC profile substantially as shown in Figure 4.

47. A substantially pure preparation of cannabidiolic acid (CBDA) substantially as described herein and having an HPLC profile substantially as shown in Figure 5.

48. A substantially pure preparation of Δ^9 tetrahydrocannabinol (Δ^9 THC) having a chromatographic purity of >99% by area normalisation of an HPLC profile.

49. A preparation according to claim 48 which is a semi-solid at room temperature.

50. A preparation according to claim 48 or claim 49 which comprises less 0.5%, preferably than 0.4%, more preferably less than 0.2% or most preferably less than 0.1% CBD (w/w).

51. A preparation according to any one of claims 48 to 50 which comprises less than 0.5%, preferably less than 0.4%, more preferably less than 0.2% or most preferably less than 0.1% CBN (w/w).

52. A preparation according to any one of claims 48 to 51 which is obtainable from cannabis plant material using a method comprising:

i) obtaining an ethanolic solution of a botanical drug substance from decarboxylated cannabis plant material,
ii) passing the solution obtained in step i) through a column of activated charcoal, and collecting the eluate,
iii) remove solvent from the eluate by rotary evaporation to give a Δ^9 THC enriched fraction,
iv) passing a solution of the resulting Δ^9 THC enriched extract through a column packed with Sephadex LH20, eluting with 2:1 chloroform/dichloromethane,
v) collecting Δ^9 THC rich fractions and removing solvent by rotary evaporation,
vi) re-dissolving the crude Δ^9 THC prepared in step v) in methanol, removing insoluble residue by filtration and removing solvent from filtrate by rotary evaporation,
vii) re-dissolving the crude Δ^9 THC prepared in step vi) in pentane, removing insoluble residue by filtration and removing solvent from the filtrate by rotary evaporation to give a semi-solid preparation of Δ^9 THC.

53. A preparation according to claim 52 wherein the ethanolic solution of a botanical drug substance from decarboxylated cannabis plant material is obtained by a method comprising the following steps:

i) harvesting cannabis plant material,
ii) decarboxylation of the plant material,
iii) extraction with liquid carbon dioxide (CO_2), removal of CO_2 to recover crude extract,
iv) dissolution of crude extract in ethanol followed by chilling of the solution to precipitate unwanted waxes,
v) removal of unwanted waxy material by cold filtration.

54. A substantially pure preparation of Δ^9 tetrahydrocannabinol (Δ^9 THC) substantially as described herein and having an HPLC profile substantially as shown in Figure 8.

55. A substantially pure preparation of Δ^9 tetrahydrocannabivarin (Δ^9 THCV) having a chromatographic purity of greater than 95%, more preferable greater than 96%, more preferable greater than 97%, more preferable greater than 98%, and most preferable greater than 99% by area normalisation of an HPLC profile.

56. A preparation according to claim 55 which is a crystalline solid at room temperature.

57. A preparation according to claim 55 or claim 56 which comprises less than 1%, preferably less than 0.8%, more preferably less than 0.6%, more preferably less than 0.4%, more preferably less than 0.2% or most preferably less than 0.1% CBD (w/w).

58. A preparation according to any one of claims 55 to 57 which comprises less than 2.0%, preferably less than 1.5%, more preferably less than 1.0% or most preferably 0.5% or less Δ^9 THC (w/w).

59. A preparation according to any one of claims 55 to 58 which comprises less than 1%, preferably less than 0.8%, more preferably less than 0.6%, more preferably less than 0.4%, more preferably less than

0.2% or most preferably less than 0.1% CBN (w/w).

60. A preparation according to any one of claims 55 to 59 which is obtainable from cannabis plant material using a method comprising:
i) obtaining an ethanolic solution of a botanical drug substance from cannabis plant material,
ii) passing the solution obtained in step i) through a column of activated charcoal, and collecting the eluate,
iii) remove solvent from the eluate by rotary evaporation to give a Δ^9 THCV enriched fraction,
iv) passing a solution of the resulting Δ^9 THCV enriched extract through a column packed with Sephadex LH20, eluting with 2:1 chloroform/dichloromethane,
v) collecting Δ^9 THCV rich fractions and removing solvent by rotary evaporation,
vi) re-dissolving the crude Δ^9 THCV prepared in step v) in methanol, removing insoluble residue by filtration and removing solvent from filtrate by rotary evaporation,
vii) re-dissolving the crude Δ^9 THCV prepared in step vi) in pentane, removing insoluble residue by filtration and removing solvent from the filtrate by rotary evaporation to give crystals of Δ^9 THCV.

61. A preparation according to claim 60 wherein the ethanolic solution of a botanical drug substance from decarboxylated cannabis plant material is obtained by a method comprising the following steps:

i) harvesting cannabis plant material,
ii) extraction with liquid carbon dioxide (CO_2), removal of CO_2 to recover crude extract,
iii) dissolution of crude extract in ethanol followed by chilling of the solution to precipitate unwanted waxes,
vi) removal of unwanted waxy material by cold filtration.

62. A substantially pure preparation of Δ^9

tetrahydrocannabivarin (Δ^9 THCV) substantially as described herein and having an HPLC profile substantially as shown in Figure 11.

63. A product enriched in cannabigerol (CBG) having a chromatographic purity of greater than 90%, preferably greater than 92% by area normalisation of an HPLC profile.

64. A product according to claim 63 which is an orange-yellow semi-solid at room temperature.

65. A product according to claim 63 or claim 64 which comprises less than 1%, preferably less than 0.8%, more preferably less than 0.6%, more preferably less than 0.4%, more preferably less than 0.2% or most preferably less than 0.1% CBD (w/w).

66. A product according to any one of claims 63 to 65 which comprises less than 1%, preferably less than 0.8%, more preferably less than 0.6%, more preferably less than 0.4%, more preferably less than 0.2% or most preferably 0.1% or less Δ^9 THC (w/w).

67. A product according to any one of claims 63 to 66 which comprises less than 1%, preferably less than 0.8%, more preferably less than 0.6%, more preferably less than 0.4%, more preferably less than 0.2% or most preferably less than 0.1% CBN (w/w).

68. A substantially pure preparation of cannabigerol (CBG) having a chromatographic purity of greater than 92%, more preferably greater than 94%, more preferably greater than 96% or most preferably greater than 97% by area normalisation of an HPLC profile.

69. A preparation according to claim 68 which is a clear colourless solution at room temperature.

70. A preparation according to claim 68 or claim

69 which comprises 4% or less, more preferably 3% or less, or most preferably less than 2% CBD (w/w).

71. A preparation according to any one of claims 68 to 70 which comprises less than 1%, preferably less than 0.8%, more preferably less than 0.6%, more preferably less than 0.4%, more preferably less than 0.2% or most preferably less than 0.1% Δ^9-THC (w/w).

72. A preparation according to any one of claims 68 to 71 which comprises less than 1%, preferably less than 0.8%, more preferably less than 0.6%, more preferably less than 0.4%, more preferably less than 0.2%, or most preferably less than 0.1% CBN (w/w).

73. A product according to any one of claims 63 to 72 which is obtainable from cannabis plant material using a method comprising:
i) decarboxylating the cannabis plant material,
ii) preparing an extract of the decarboxylated cannabis plant material with hexane,
iii) filtering the resultant extract and removing solvent from filtrate by rotary evaporation to form an extract enriched in CBG,
iv) passing a solution of the resulting CBG enriched extract through a column packed with Sephadex-LH20™, eluting with 2:1 chloroform/dichloromethane,
v) collecting CBG rich fractions eluted from the column and removing solvent by rotary evaporation,
vi) re-dissolving the crude CBG obtained in step v) in methanol, removing insoluble residue by filtration and removing solvent from filtrate by rotary evaporation,
vii) re-dissolving the product of step vi) in pentane, removing insoluble residue by filtration and removing solvent from filtrate by rotary evaporation to produce a highly enriched CBG extract or substantially pure cannabigerol.

74. A product according to claim 73 wherein the method includes a further step viii) of loading the

highly enriched CBG extract or substantially pure cannabigerol onto a Chromabond Flash BT 12M silica cartridge column, and eluting with hexane:ethyl acetate (98:2) at a flow rate of approximately 5 ml/min.

75. A product enriched in cannabigerol (CBG) substantially as described herein and having an HPLC profile substantially as shown in Figure 14.

76. A substantially pure preparation of cannabigerol (CBG) substantially as described herein and having an HPLC profile substantially as shown in Figure 15.

77. A substantially pure preparation of cannabigerol (CBG) substantially as described herein and having an HPLC profile substantially as shown in Figure 16.

78. A product enriched in cannabichromene (CBC) having a chromatographic purity of greater than 80%, more preferably greater than 85% by area normalisation of an HPLC profile.

79. A product according to claim 78 which is an orange-yellow semi-solid at room temperature.

80. A product according to claim 78 or claim 79 which comprises less than 5%, preferably less than 4%, more preferably less than 3%, more preferably less than 2% or most preferably 1% or less CBD (w/w).

81. A product according to any one of claims 78 to 80 which comprises less than 2%, preferably less than 1.5%, more preferably less than 1.0%, more preferably less than 0.5% or most preferably 0.3% or less Δ^9 THC (w/w).

82. A product according to any one of claims 78 to 81 which comprises less than 1%, preferably less

than 0.8%, more preferably less than 0.6%, more preferably less than 0.4%, more preferably less than 0.2% or most preferably 0.1% or less CBN (w/w).

83. A substantially pure preparation of cannabichromene (CBC) having a chromatographic purity of greater than 85%, more preferably greater than 90%, more preferably greater than 95%, more preferably greater than 98% or most preferably greater than 99% by area normalisation of an HPLC profile.

84. A preparation according to claim 83 which is a clear colourless solution at room temperature.

85. A preparation according to claim 83 or claim 84 which comprises 1% or less, more preferably 0.8% or less, more preferably 0.6% or less, more preferably 0.4% or less or most preferably less than 0.2% CBD (w/w).

86. A preparation according to any one of claims 83 to 85 which comprises less than 1%, preferably less than 0.8%, more preferably less than 0.6%, more preferably less than 0.4%, more preferably less than 0.2% or most preferably less than 0.1% Δ^9-THC (w/w),

87. A preparation according to any one of claims 83 to 86 less than 1%, preferably less than 0.8%, more preferably less than 0.6%, more preferably less than 0.4%, more preferably less than 0.2% or most preferably less than 0.1% CBN (w/w).

88. A product according to any one of claims 78 to 87 which is obtainable from cannabis plant material using a method comprising:
i) decarboxylating the cannabis plant material,
ii) preparing an extract of the decarboxylated cannabis plant material with hexane,
iii) filtering the resultant extract and removing solvent from filtrate by rotary evaporation to form an extract enriched in CBC,

iv) passing a solution of the resulting CBC enriched extract through a column packed with Sephadex-LH20™, eluting with 2:1 chloroform/dichloromethane,
v) collecting CBC rich fractions eluted from the column and removing solvent by rotary evaporation,
vi) re-dissolving the crude CBC obtained in step v) in methanol, removing insoluble residue by filtration and removing solvent from filtrate by rotary evaporation,
vii) re-dissolving the product of step vi) in pentane, removing insoluble residue by filtration and removing solvent from filtrate by rotary evaporation to produce a highly enriched CBC extract.

89. A product enriched in cannabichromene (CBC) substantially as described herein and having an HPLC profile substantially as shown in Figure 19.

90. A substantially pure preparation of cannabichromene (CBC) substantially as described herein and having an HPLC profile substantially as shown in Figure 20.

91. A method according to claim 1 which comprises a further step v) of:
v) loading the substantially pure cannabinoid or cannabinoid acid or the product enriched in a given cannabinoid or cannabinoid acid onto a Chromabond Flash BT 12M silica cartridge column, eluting with hexane:ethyl acetate (98:2) at a flow rate of approximately 5 ml/min.